REMARKS

Claims 26 and 33 to 52 are pending in this application. Claims 26 and 33 to 52 stand finally rejected under 35 U.S.C. §112, first paragraph. Applicants acknowledge withdrawal of the rejection of claims 26 and 33 to 52 under 35 U.S.C. §112, second paragraph and under the judicially-created doctrine of obviousness-type double patenting. Applicants are herein amending claim 26, without prejudice or disclaimer.

Amendments to Claims

Applicants are herein amending claim 26 to recite that the method of the invention is useful in treating Alzheimer's disease and conditions relating to appetite control, thermoregulation, and sleep. Applicants submit that no new matter is introduced by the amendment. Support may be found in the specification on, *inter alia*, page 11, lines 10 to 17. Applicants reserve the right to file one or more continuing application directed to the deleted subject matter of claim 26.

Applicants request entry of the amendment under 37 C.F.R. § 1.116(b) because the amendments to the claims either cancel claims, comply with requirements of form expressly set forth in a previous Office Action, or present the rejected claims in better form for consideration on appeal.

Rejection under 35 U.S.C. § 112, first paragraph

In the Office Action, claims 26 and 33 to 52 are rejected under 35 U.S.C. § 112, first paragraph as allegedly being non-enabled, specifically with methods of treating neurodegenerative disease, eating disorders, disorders of thermoregulation, sleep dysfunction, and sexual dysfunction. While applicants continue traverse the rejection and believe that the claims are fully enabled, applicants are herein amending claim 26 to specify that the compounds of formula I are useful in methods of treating a subject suffering from a condition

selected from the group consisting of Alzheimer's disease, appetite control, disorders of thermoregulation, and sleep dysfunction.

Applicants submit that the specification enables a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and to use the invention commensurate in scope with claims 26 and 33 to 52, as amended.

There is a nexus between antagonist activity at brain 5-HT_{1A} serotonin receptors and the treatment of Alzheimer's disease, appetite control, disorders of thermoregulation, and sleep dysfunction. Applicants have provided procedures for two assays to evaluate activity of the compounds of the invention in the specification on page 9, line 1 to page 10, line 23. The first assay is the 3H-paroxetine binding assay, which assesses affinity of drugs for the serotonin transporter. The second assay assesses the agonism/antagonism at the 5-HT_{1A} receptor using [35S]-GTPγS binding to cloned human 5-HT1A receptors. Applicants have also provided data on page 11, lines 1 to 8 to show that representative compounds of the invention have potent affinity for and antagonist activity at brain 5-HT_{1A} serotonin receptors.

As 5-HT_{1A} serotonin receptor antagonists, the compounds of formula I are expected to be useful for the treatment of Alzheimer's disease and in the control of various physiological phenomena, such as appetite control, thermoregulation, and sleep, which are known to be, at least in part, under serotonergic influence (page 11, lines 15 to 17). ***This nexus is recognized in the art.*** See, for example,

Condition	***Reference showing nexus 5-HT_{1A} antagonist and condition***
Alzheimer's disease	Lanfumey, *et al., Current Drug Targets – CNS & Neurological Disorders* (**2004**) *3*:1-10 (See page 5 in particular) Kwon, *et al., Neurodegenerative Dis.* (**2004**) 1:113-52 (See page 145 and 147)
Appetite control	Moreau, *et al., Brain Res. Bull.* (**1992**) 29(*6*): 901-4
Disorders of thermoregulation	Ootsuka, *et al., J. Physiol.* (**2003**) 552(*1*): 303-14
Sleep dysfunction	Sorensen, *et al.,Behav. Brain Res.* (**2001**) 121(*1-2*): 181-7

Contrary to the assertion in the Office Action, the *Barnes* reference does not sufficiently establish that 5-HT_{1A} antagonist do not function in thermoregulatory control.

Rather the reference states that there appears to a species difference (*i.e.*, between rats and mice) in the mechanism underlying the hypothermic effect of 5-HT_{1A} receptor agonists; in the mouse it appears presynaptic, whereas in the rat it can be mediated via both pre- and postsynaptic mechanisms. What *Barnes*, however, does explicitly state is that the role of the "5-HT_{1A} receptors in many of these response is clear" with reference to hyperphagia, hypothermia, altered sexual behavior, tail flick response, anxiety, and depression. Accordingly, there is no reason to doubt that the compounds of formula I and every reason to believe that the compounds of formula I (as 5-HT_{1A} antagonists) would be useful in the treatment of conditions relating appetite control and thermoregulation.

Because there is a established nexus between compounds having 5-HT_{1A} antagonist activity and methods of treating Alzheimer's disease and condition relating to appetite control, thermoregulation, and sleep, applicants respectfully submit that there is not a reasonable basis for rejecting the claims. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims, as amended, under 35 U.S.C. § 112, first paragraph.

Conclusions

Applicants respectfully request reconsideration and withdrawal of the rejection of the claims in view of the remarks. If the Examiner has any questions, the Examiner is invited to call the undersigned at (215) 557-3861.

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